ABSTRACT

Novel methods for identification of inhibitors or modulators of binding activities mediated by lectin domains of polypeptide GalNAc-transferases are disclosed. Direct binding activity of GalNAc-transferase lectins has been demonstrated for the first time and methods to measure lectin mediated binding of isolated lectins or enzymes with lectin domains are disclosed. The present invention specifically discloses a novel selective inhibitor of polypeptide GalNAc-transferase lectin domains, which provides a major advancement in that this inhibitor and related inhibitors sharing common characteristics of activity bind lectin domains without serving as acceptor substrate for glycosyltransferases involved in synthesis of O-glycans. This inhibitor is represented by the β-anomeric configuration of GalNAc-benzyl, GalNAcβ-benzyl. Methods for inhibiting intracellular transport, cell surface expression, and secretion of mucins and O-glycosylated glycoproteins without affecting O-glycosylation processing are disclosed using the novel selective inhibitor identified.